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Medical Economics · July through December 1966

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"I suggest, Miss Pomeroy, that you shorten your engagement."

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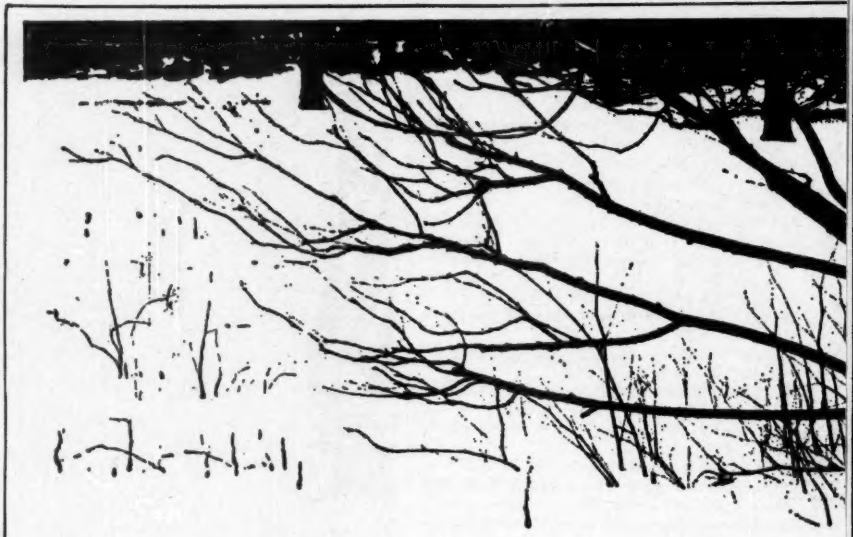

Life can seem bleak to some anxious cardiac patients.

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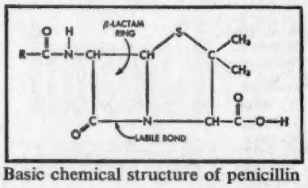
Penicillin G and the penicillinase resistant semisynthetics—

consider the differences in pharmacologic action, in antibacterial effect

Within the last decade few molecules have been as vigorously investigated as that of penicillin. The result—new semisynthetic penicillins with differences in their actions on bacteria and their interactions with the host. These differences may greatly affect their use in clinical practice.

In the October 16, 1965 issue of the Journal of the Canadian Medical Association, Dr. H. Kalant[1] of the Department of Pharmacology of the University of Toronto discusses the theoretical basis for these differences.

Destruction of Bacteria



Basic chemical structure of penicillin

The basic structure of penicillin is 6-aminopenicillanic acid.

The important part of the penicillin molecule, as far as antibacterial action is concerned, is the highly reactive and relatively unstable beta-lactam ring.

This is how it may react with bacteria:

Bacteria are surounded by a rigid outer wall which is continually being synthesized from within. The synthesized material is transferred by enzyme action to the outer wall.

When penicillin comes into contact with susceptible bacteria, the labile bond in the C-N linkage of the beta-lactam ring breaks. The C attaches itself to receptor sites on the transferring enzymes of the bacteria, preventing further synthesis of the outer wall. Without the protection of the outer wall, the bacteria rupture from internal osmotic pressure.

Penicillin and penicillinase

Apparently the beta-lactam ring is the key to effective antibacterial action. But it is also the key to the inactivation of penicillin.

Certain bacteria (resistant staph, for example) produce the enzyme penicillinase. When penicillinase comes into contact with penicillin it breaks the C-N linkage of the beta-lactam ring. The C reacts with the penicillinase to form penicilloic acid. Since the C is no longer free to react with the bacterial enzymes, there can be no destruction of the bacteria and the enzymatic action of penicillinase remains unchanged.

Penicillinase is counteracted by certain semisynthetics

Modifications to the R side chain of the molecule alter the reactivity of the penicillin—either by altering the stability of the beta-lactam ring or by protecting the labile C-N bond from hydrolysis by penicillinase.

The newer semisynthetic penicillins protect the C-N bond with bulky R groups arranged to shield it from the action of penicillinase. This process is called steric hindrance.

Some semisynthetic penicillins, when they come into contact with the penicillinase, bind themselves to the penicillinase, altering the penicillinase as they lose their activity.

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